



Armed Forces College of Medicine

AFCM



HEPATITIS VIRUSES (Part 1)

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By the end of this lecture the student will be able to :

1. Describe the structure of hepatitis viruses
2. Describe pathogenesis & clinical manifestations of hepatitis viruses
3. Describe laboratory diagnosis of hepatitis viruses
4. Outline prevention of hepatitis viruses

Hepatitis viruses



- Many viruses cause hepatitis
- **Hepatitis viruses** are viruses that infect **the liver as 1ry target organ**
- **Humans are the only natural host** for hepatitis viruses

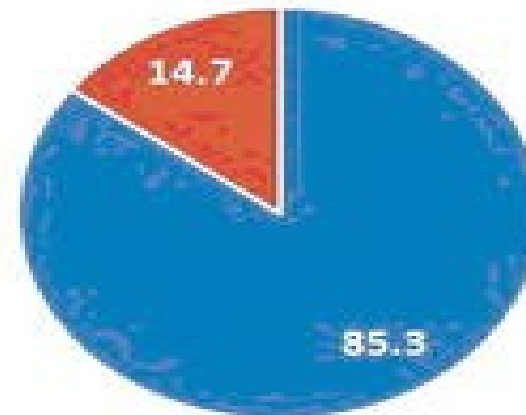
Important properties of hepatitis viruses

Virus	Family	Genome	Envelope	Modes of transmission
Hepatitis A virus (HAV)	Picornavirus	ssRNA	Non enveloped	Enteric : Fecal-oral
Hepatitis B virus (HBV)	Hepadnavirus	dsDNA	Enveloped	• Parental (injured skin & MM) • From mother to child • Sexual
Hepatitis C virus (HCV)	Flavivirus	ssRNA		

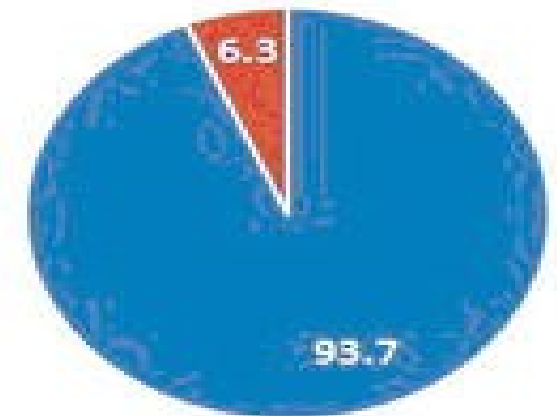
Prevalence of HCV in Egypt 2008 - 2015

Anti-HCV Antibodies (+Ve)

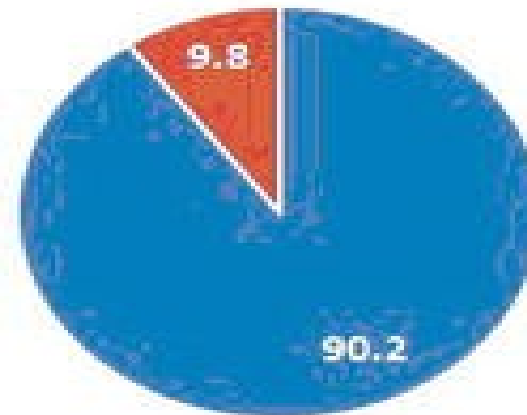
2008



2015



HCV RNA (+Ve)



Hepatitis viruses



- Some other viruses may infect the liver as **a 2ry target organ**

Virus	Family	Disease
Epstein-Barr virus (EBV)	Herpesvirus	Infectious mononucleosis
Cytomegalo virus (CMV)	Herpesvirus	Infectious mononucleosis
Yellow fever virus (YFV)	Flavivirus GIT Module	Hemorrhagic fever



Hepatitis B Virus

Structure

A-Nucleocapsid (HBV)

1-Genome : Partially dsDNA.

2- DNA polymerase enzyme

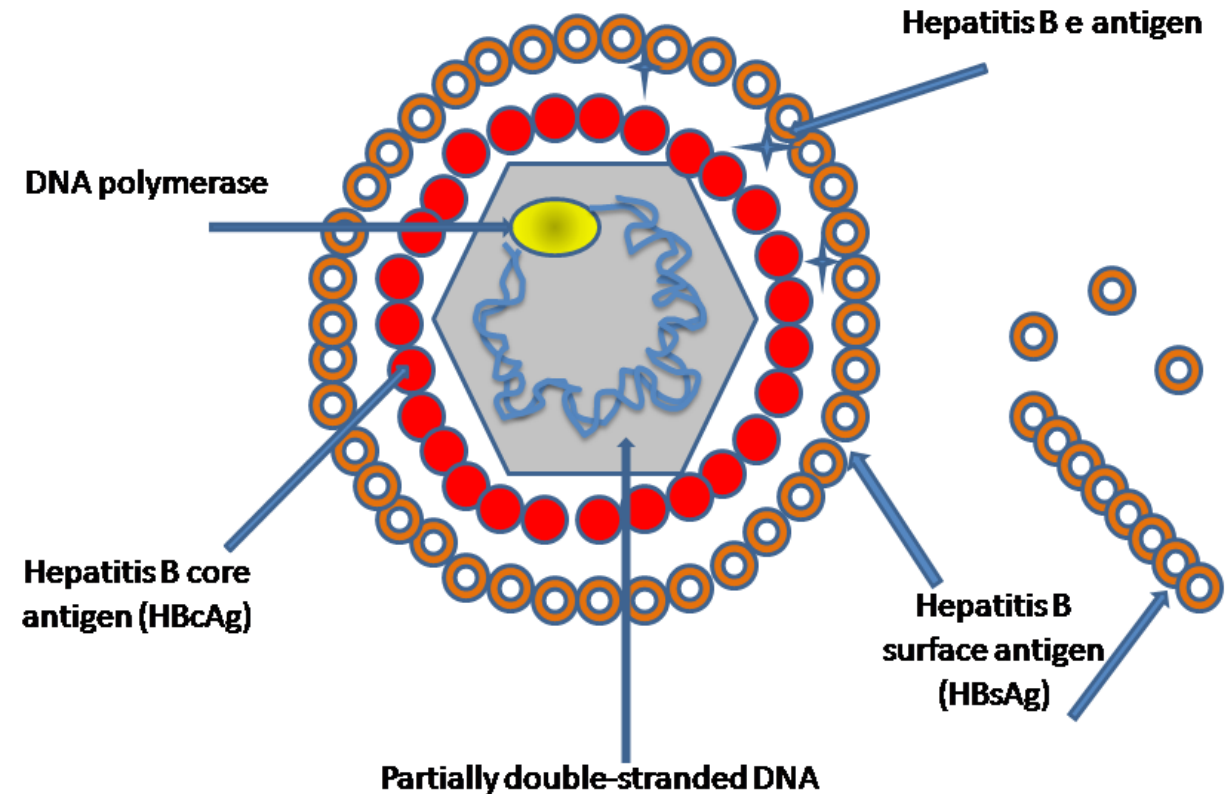
3-Ags

a. **c (core) Ag**

b. **e (early) Ag**

B-Envelope

Host derived lipid part carrying **s (surface) Ag**



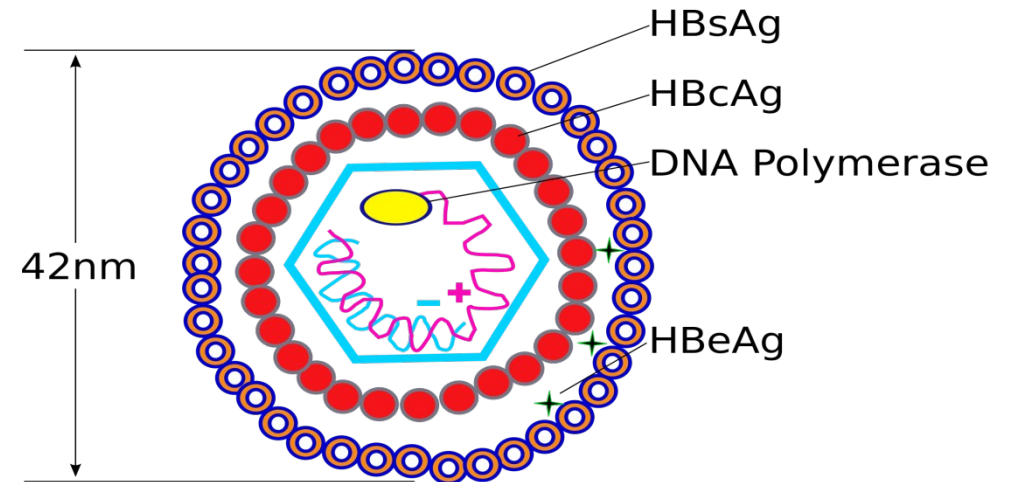
Parenterally Transmitted Hepatitis Viruses



Core Ags

a- c (core) Ag

Located on the capsid

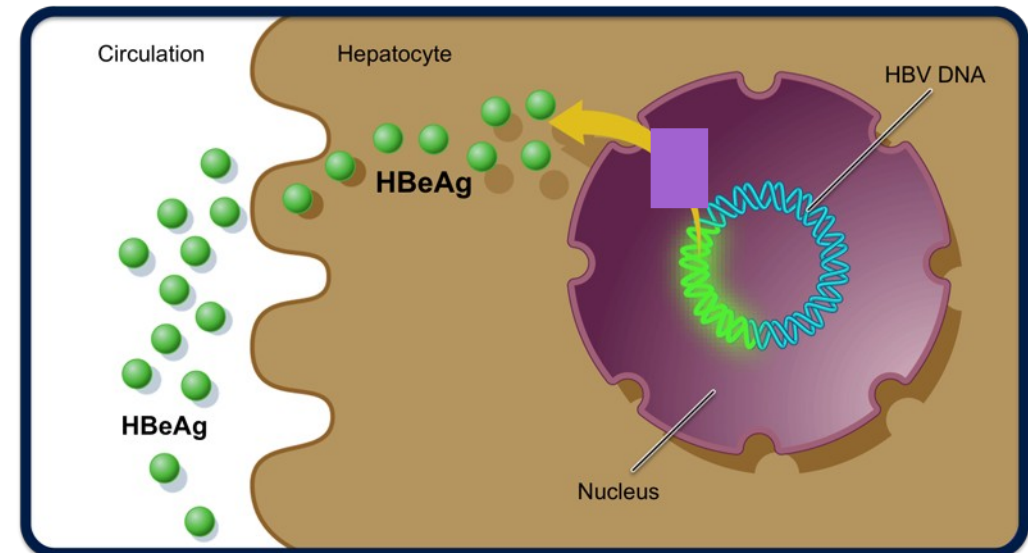


b- e (early) Ag

Soluble & secreted from infected cells
during viral replication



Not found in the virion
(or found in small amount)



Parenterally Transmitted Hepatitis Viruses



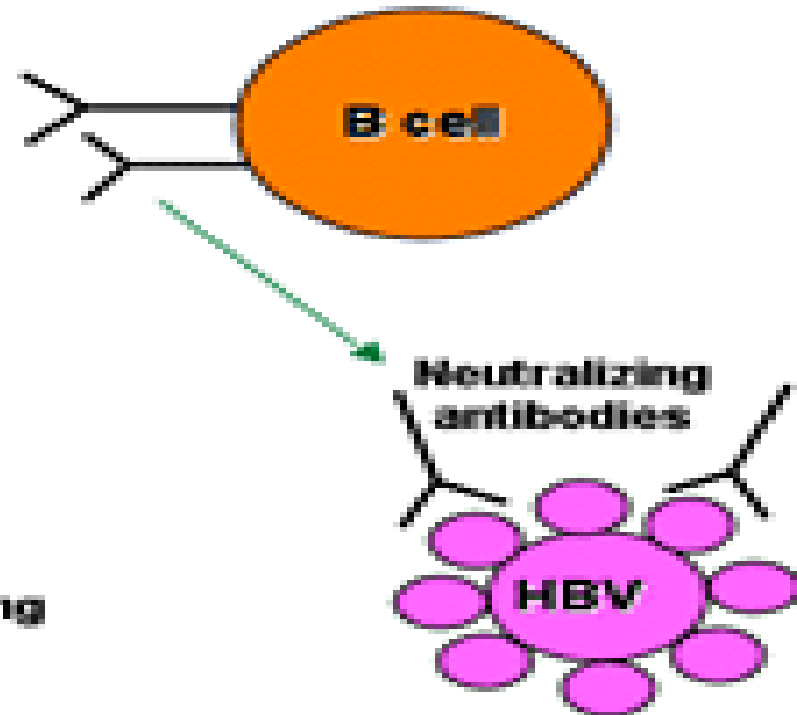
Envelope : host derived lipid part carrying **s (surface) Ag**

1- Responsible for **viral attachment to hep**

↓
○ + production of **neutralizing Abs**
↓

Long term protection against reinfection

2- Used in **vaccine preparation**



Parenterally Transmitted Hepatitis Viruses



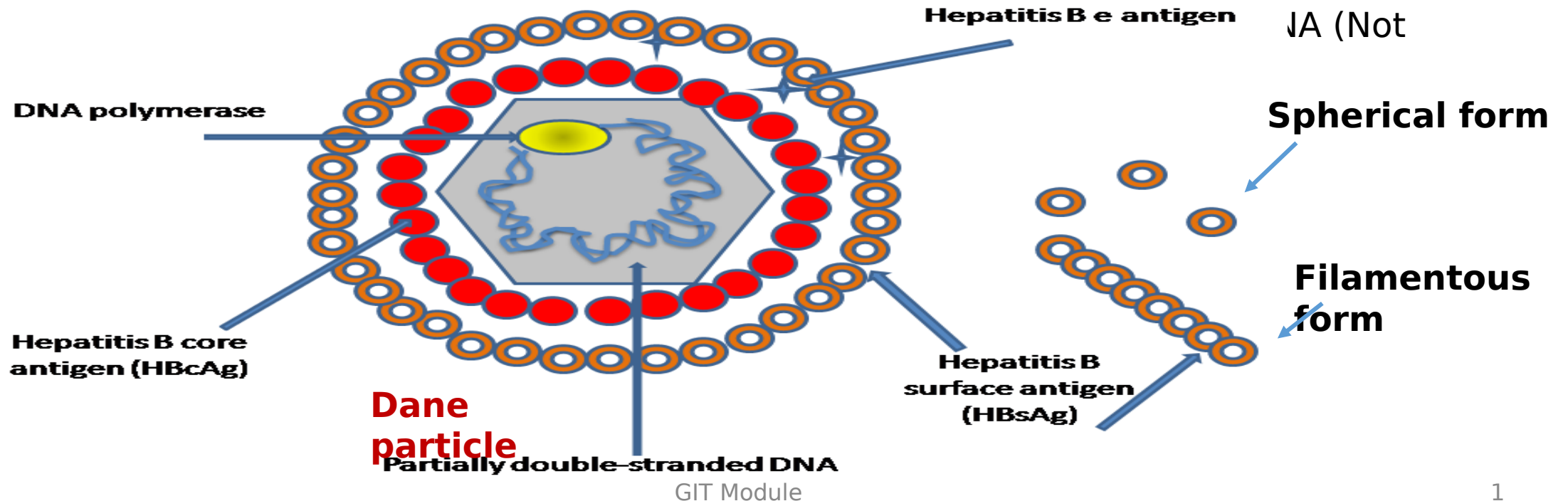
3- Expressed in **excess** & released in large amounts into blood

3 forms of HBV are detected in patient serum by EM

a-Dane particle

b-Spherical

Complete virion (infectious) Filamentous



QUIZ



1-Dane particle contains :

- a. sAg
- b. sAg + cAg.
- c. sAg + cAg + partially ds DNA.
- d. sAg + cAg + partially ds DNA + DNA polymerase
- e. sAg + cAg + ss RNA + RNA polymerase.

d

Hepatitis C Virus

Structure (HCV)

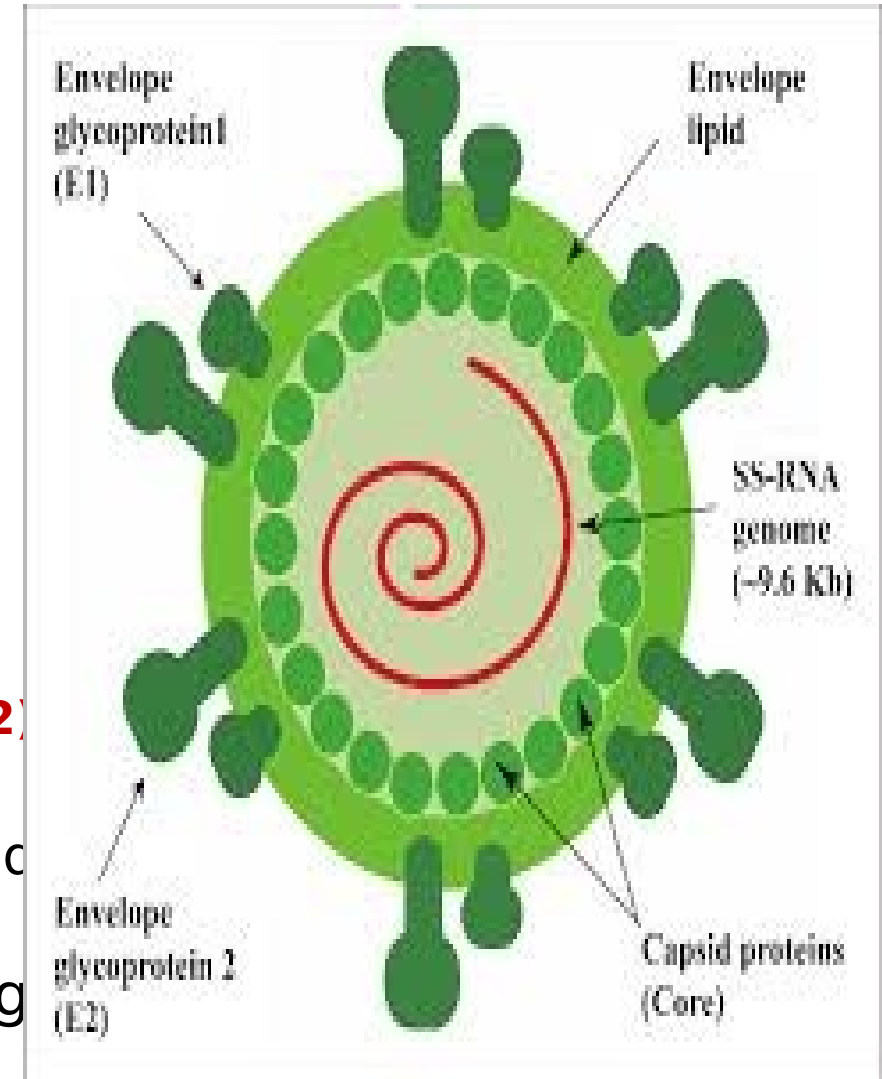
A-Nucleocapsid

1-Genome : ssRNA

■ There are **6 genotypes** based on differences in gene coding **one of the 2 envelope glycoproteins (E2)**

■ **Genotype 4 is predominant in Egypt** (followed by Genotype 1)
{ Higher resistance to antiviral drugs than other genotypes }

2-Capsid (core) protein



Parenterally Transmitted Hepatitis Viruses

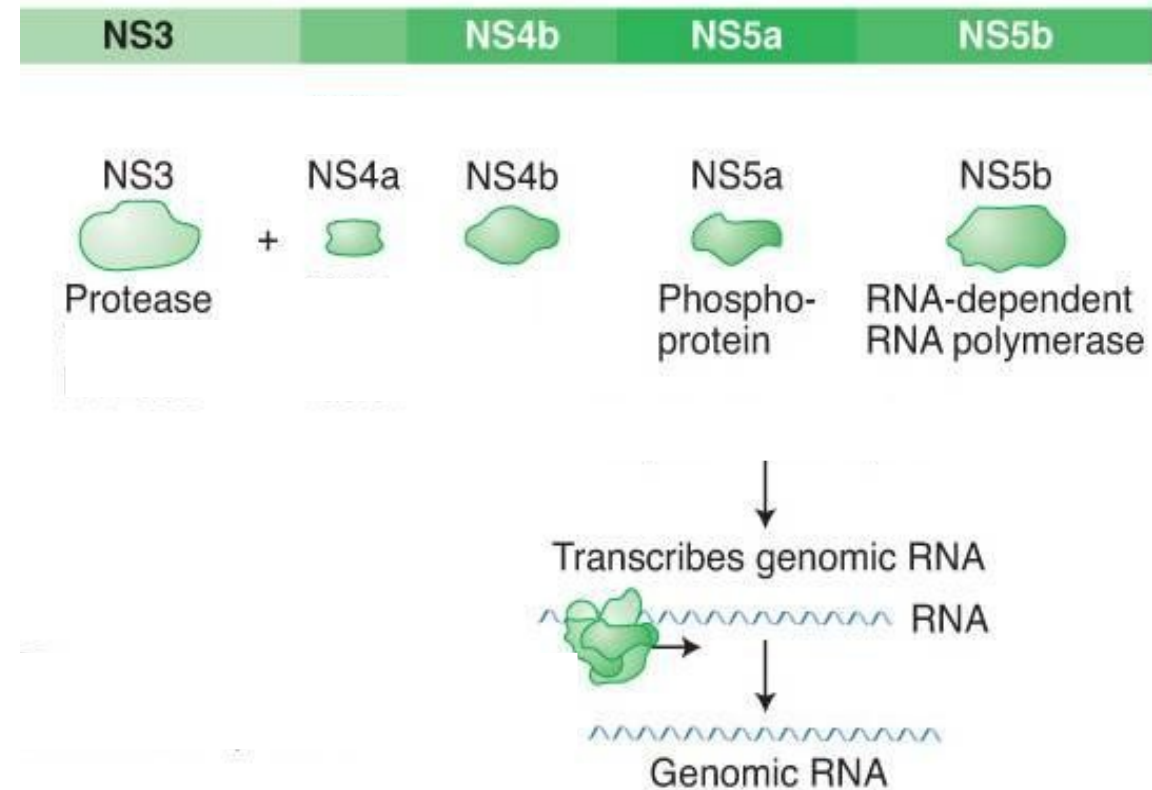
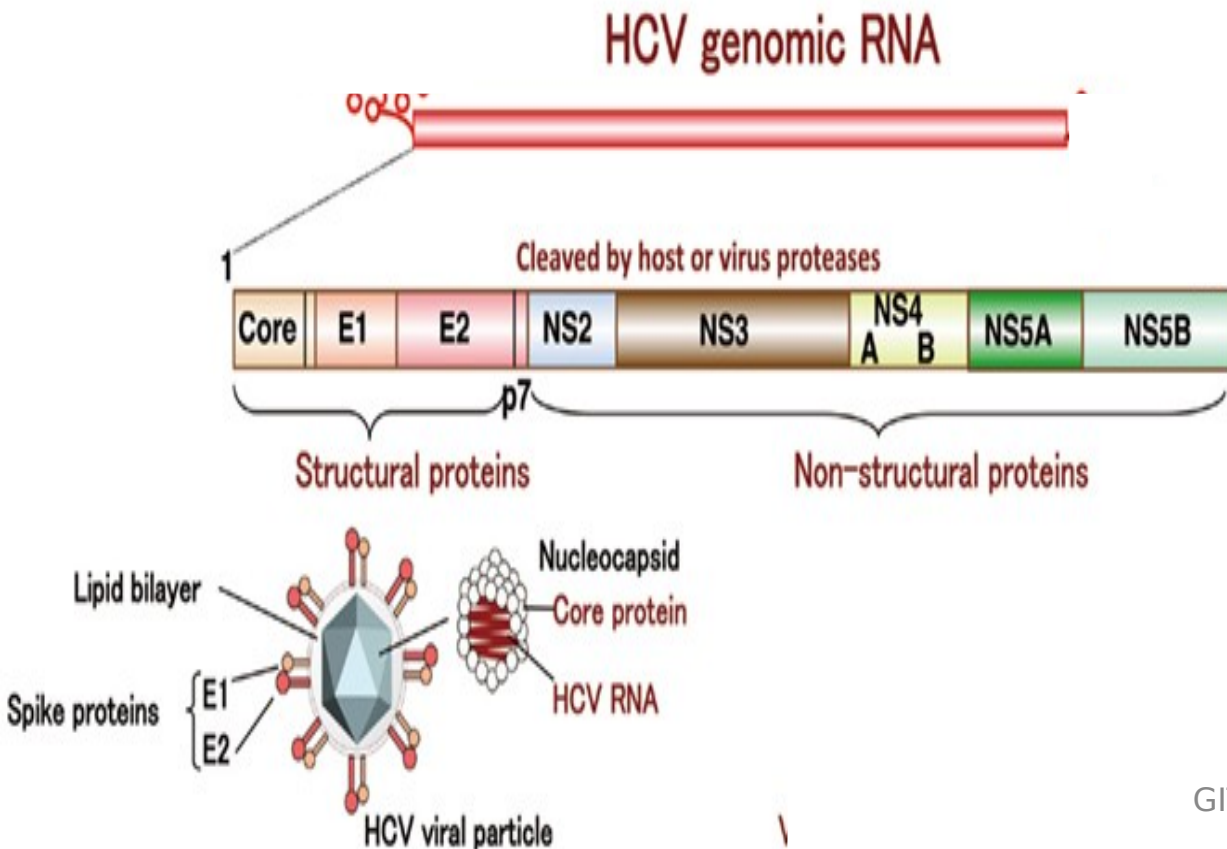


3-Enzymes involved in viral replication (Non structural proteins)

a. NS5A : **Initiates transcription** of RNA genome

Main targets for antiHCV drugs

al replication



Parenterally Transmitted Hepatitis Viruses

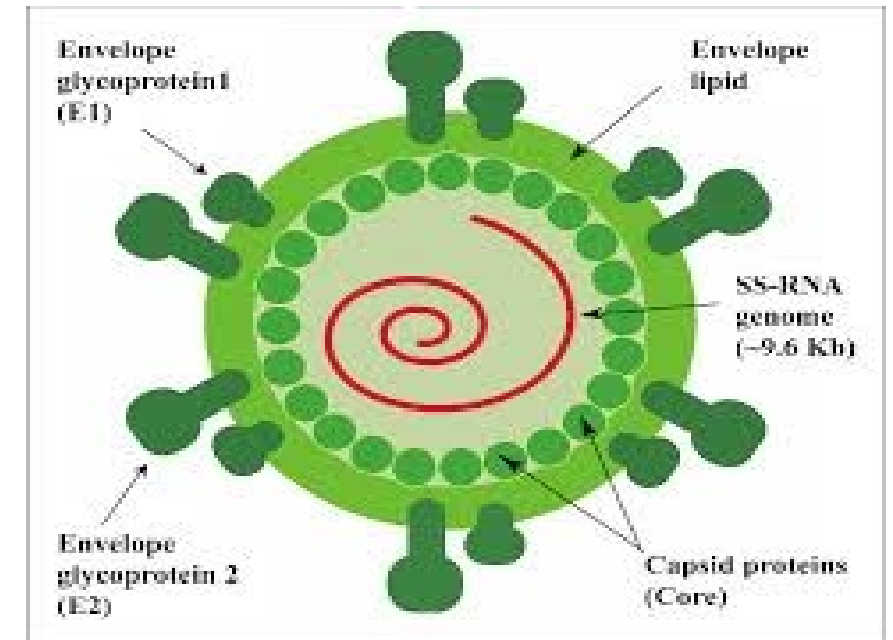
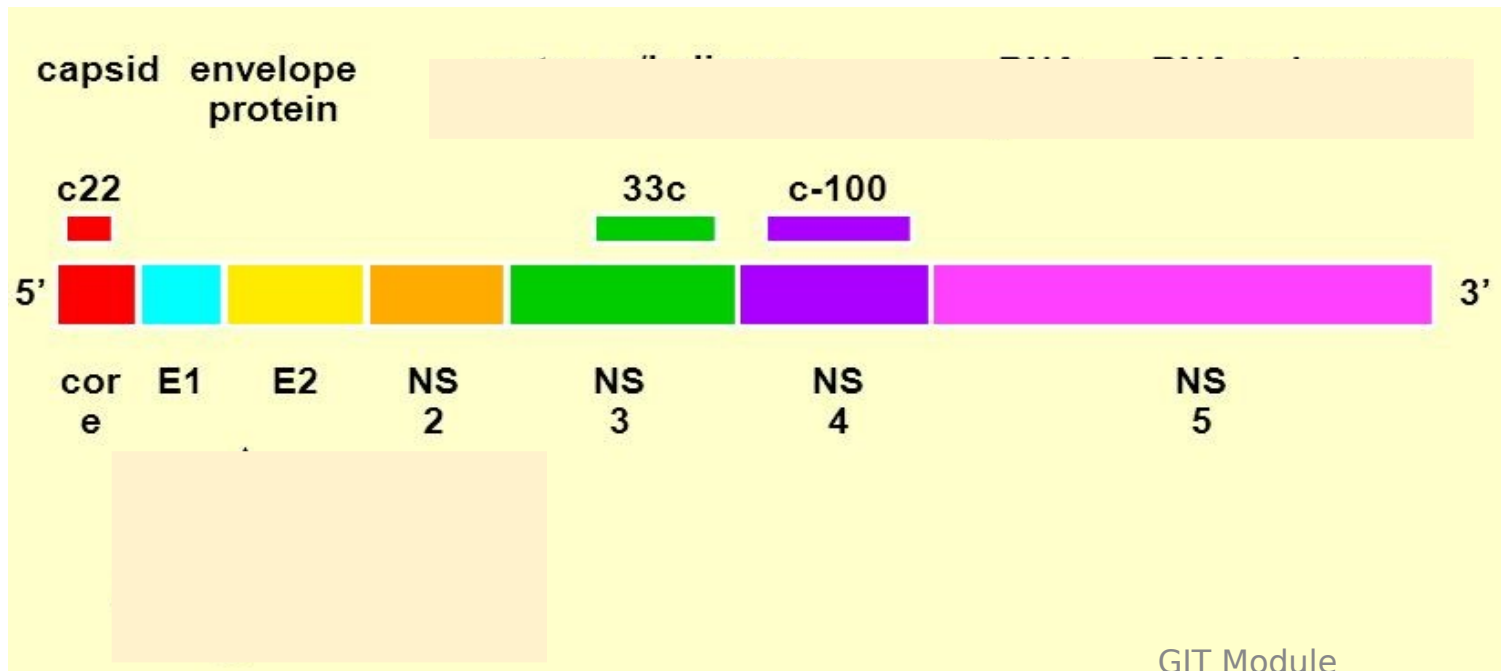


B -Envelope

Host derived lipid part carrying **2 envelope glycoproteins (E1& E2)** :

Responsible for **viral attachment** to hepatocytes

□ **E2** differs between the genotypes



Parenterally Transmitted Hepatitis Viruses



Modes of transmission of HBV&HCV

1-Parental (injured skin & MM)

a-Occupational exposure of health care workers to blood & body fluids:

Percutaneous (needle -stick injuries & contaminated sharp instruments) & permucosal (splashes to eyes)

b- Injection drug use with shared needles.

c- Tattooing, ear piercings & acupuncture.

d- Blood & blood products (clotting factors & Igs) transfusion

(uncommon due to screening of blood for HBV&HCV)

e-Hemodialysis .

f-House-hold family contacts : frequent contact with blood

(through cuts, abrasions or MM e.g sharing razors & toothbrushes)

Parenterally Transmitted Hepatitis Viruses



2-From mother to child during birth

Through contact of maternal blood with MM of baby

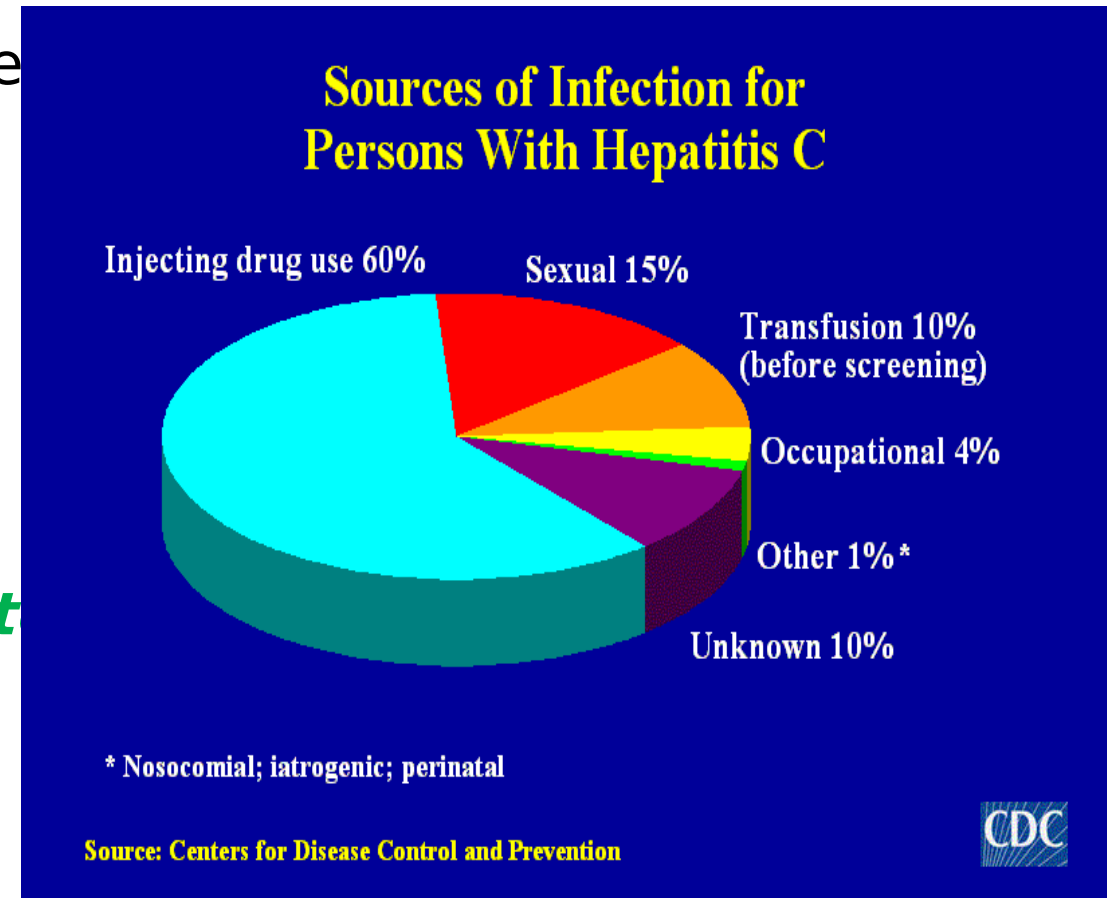
(Transplacental transmission is rare

3-Sexual transmission (uncommon in HCV).

4-Organ transplantation

NB

No documented transmission by saliva, sweat, breast milk, urine or feces



ROUTES OF TRANSMISSION

1) Vertical transmission



2) Sexual transmission



3) Parenteral transmission



Blood Transfusion



Body Piercing

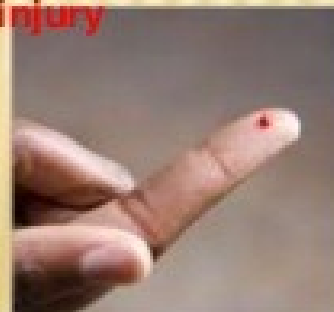


Tattooing



IV Drug Use

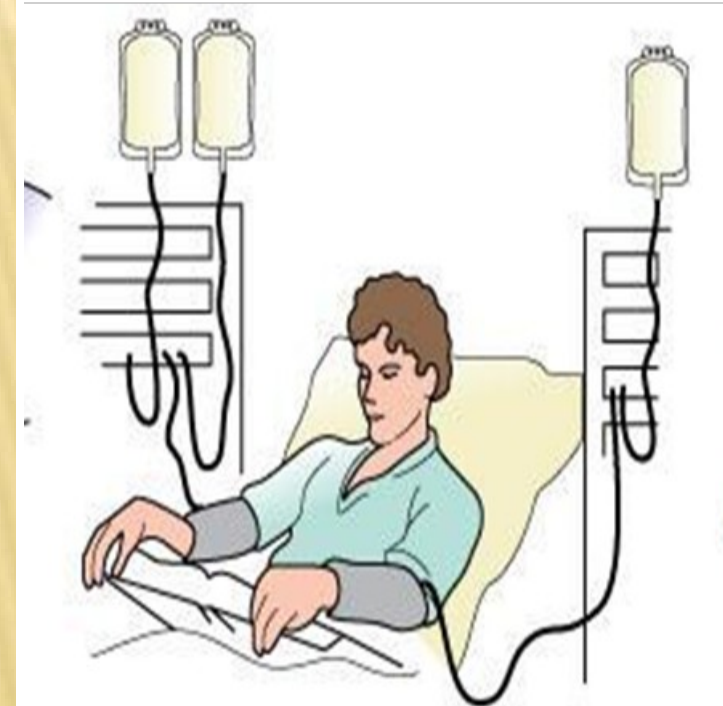
Needle stick injury



Household contacts



GIT Module



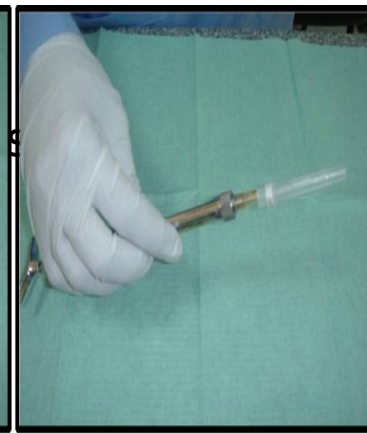
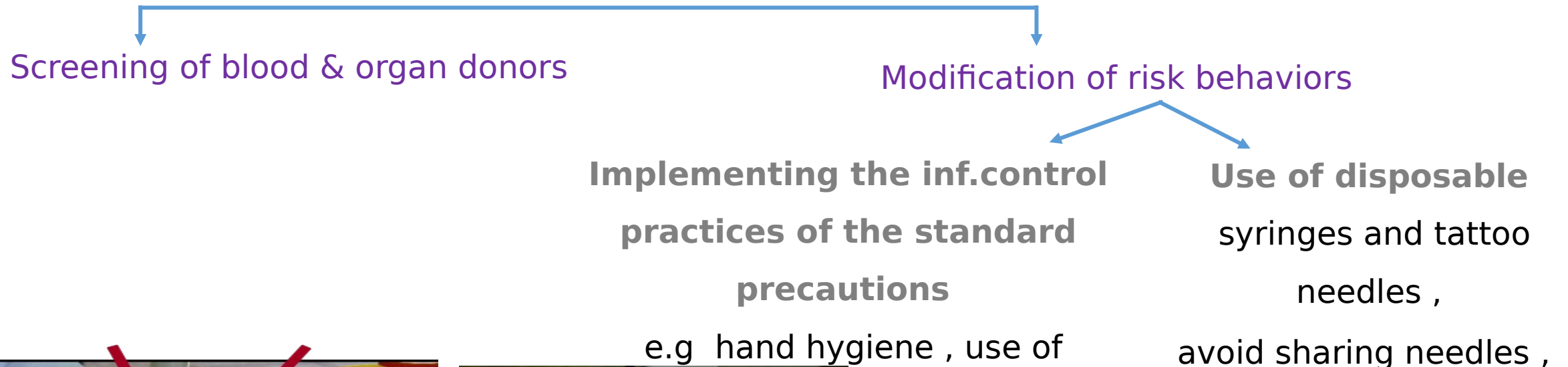
Contaminated dialysis equipment

Parenterally Transmitted Hepatitis Viruses



Prevention of HBV&HCV

I-General hygienic measures for HBV&HCV (prevent exposure)



Parenterally Transmitted Hepatitis Viruses



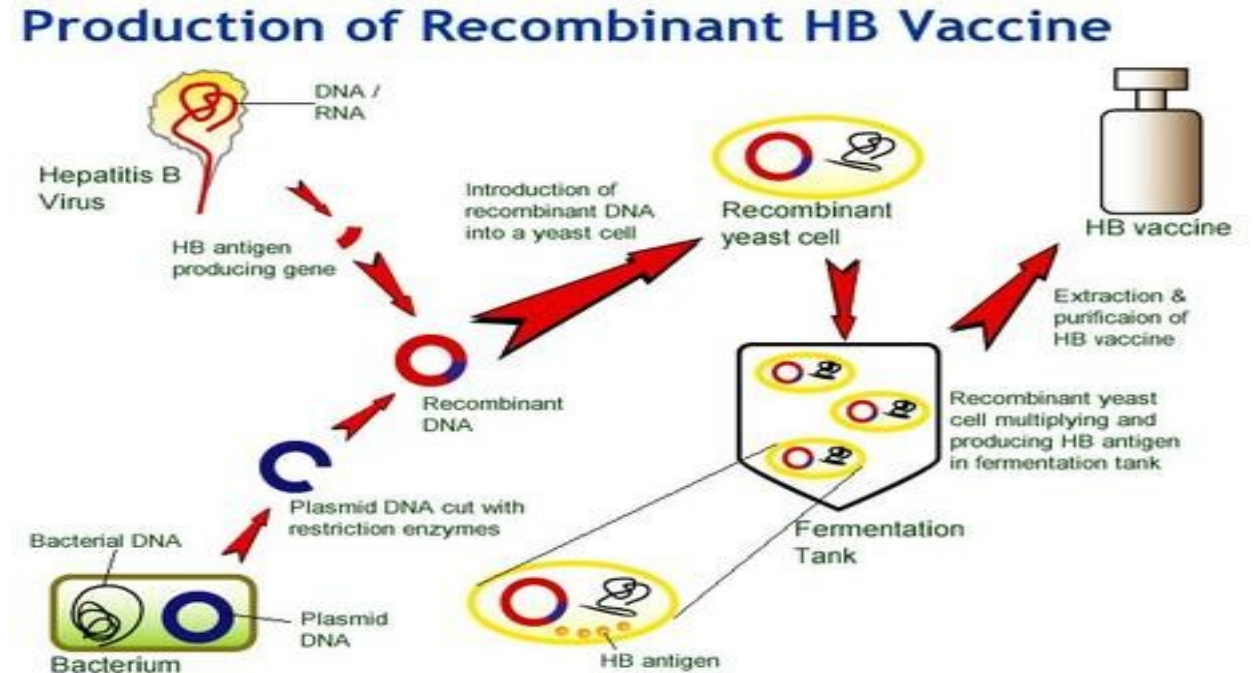
II-Immunization for HBV

A - Active immunization :

Vaccine containing sAg

(Recombivax or Engerix)

Preparation : Recombinant DNA technique



Parenterally Transmitted Hepatitis Viruses



2-Administration

3 doses :0,1&6ms.

IM

3-Indications

**Routinely to
Newborns**

(Given at 2,4&6 ms)

High risk groups (frequently exposed to blood & blood products)

Hemophilia

Hemodialysis

Health care workers :

Dentists,surgeons & lab. workers

4-Response to vaccine

A post-vaccination

anti HBs level

> 10 mIU/ml

is protective

If no response

(< 10 mIU/ml),

**3 further doses
are given**

Non responder

An individual who fails to develop immunity **after 2 vaccine courses**
Must receive *passive immunization*
on suffering accidental exposure

Parenterally Transmitted Hepatitis Viruses



II-Combined passive & active immunization : given as post exposure prophylaxis

Passive immunization : HB Immunoglobulin (HBIG) containing anti HBsAg



e.g needle prick or sharp injury

for **non vaccinated** or **non responder**

individuals +

Vaccination with HBsAg : injected simultaneously at separate

Given in **accidental exposure & to newborns of infect**





2- A 25 yr old women whose blood tested positive for HBsAg gave birth to a full term child. Which of the following therapies would be most likely to minimize the transmission of HBV to the neonate?

- a. Administer HB immunoglobulins.
- b. Administer HB vaccine.
- c. Administer HB immunoglobulins & HB vaccine.
- d. Bottle-feed the neonate.
- e. Administer interferon

Parenterally Transmitted Hepatitis Viruses



Pathogenesis of HBV

A - Modes of transmission : see before

B -Entry & Spread

Enters & spreads by blood

Viremia

Very high viral load (10^{10} /ml serum)

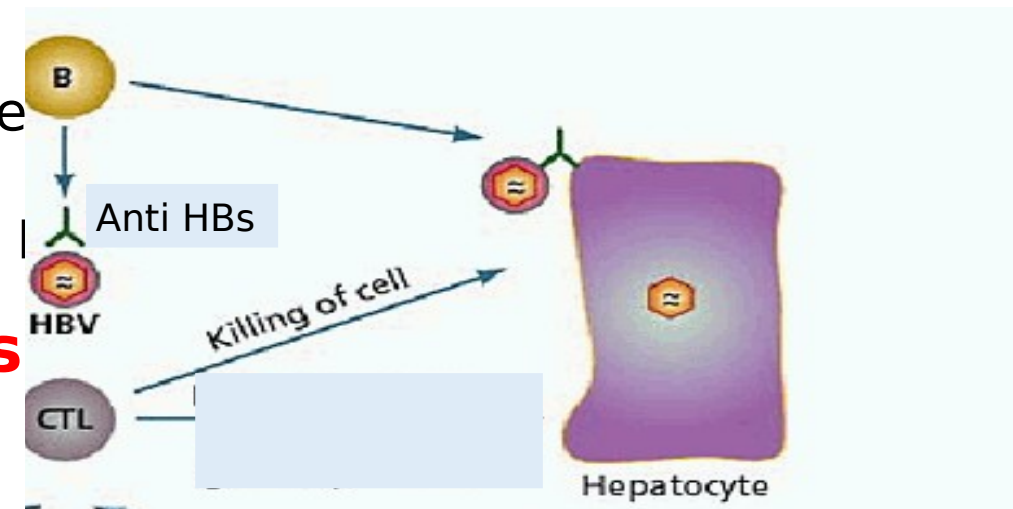
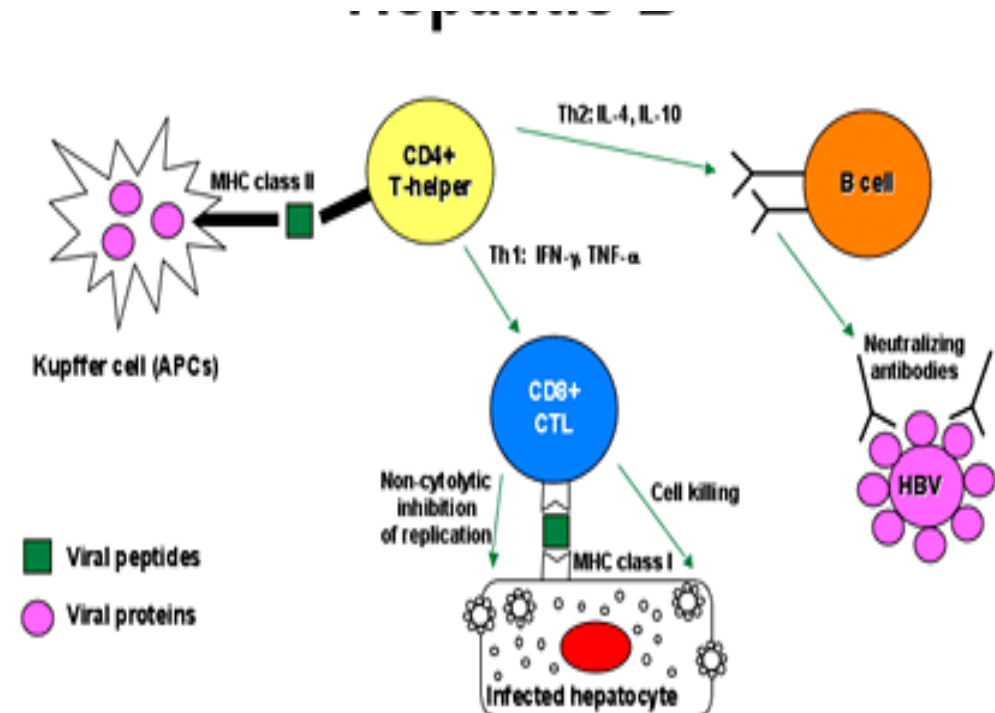
Very high rate of transmission compared to H

C -Effect on hepatocytes

Multiplies in hepatocytes **with no CPE** (cytopathic effect)

Infected cells express **viral Ags** in association with

Killed by Cytotoxic T Lymphocytes



D-Fate of infection

1-90% of adults recover completely.

2-1% develop fulminant hepatitis :

acute hepatic failure due

to **massive immune-mediated lysis** of infected hepat

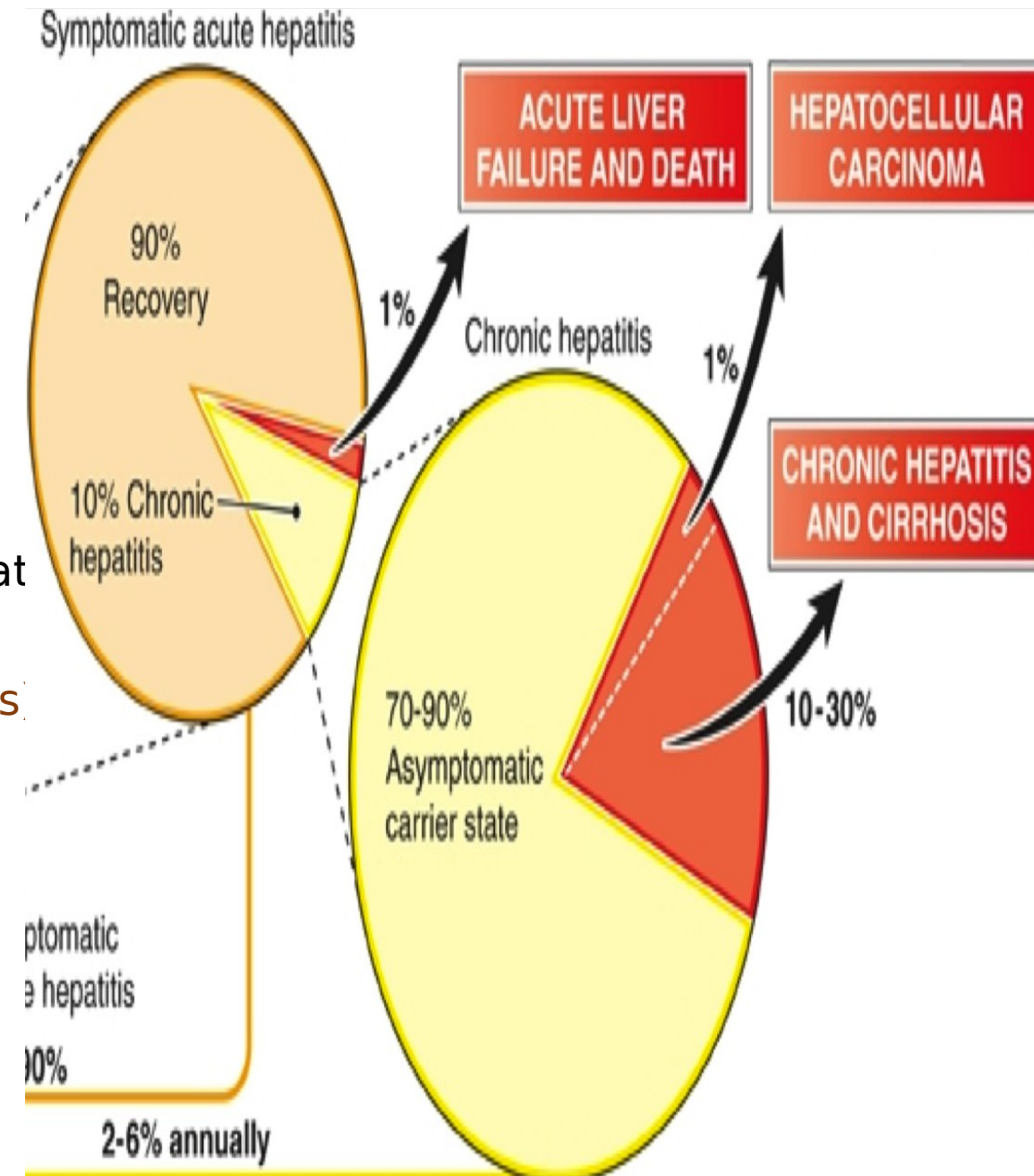
3-Chronic hepatitis (5-10 % in adults & 90% in newborns)

a.Definition : Persistence of S Ag in blood ≥ 6 ms

b.Determinant : Adequacy of **CTLs**.

4-Liver cirrhosis

5-Hepatocellular carcinoma



Pathogenesis of HCV

A-Modes of transmission : see before

B-Entry & Spread :

As HBV (**less** viral load → **less rate of transmissi**

C -Effect on hepatocytes : As HBV

D-Fate of infection

1-25-50% of adults recover completely

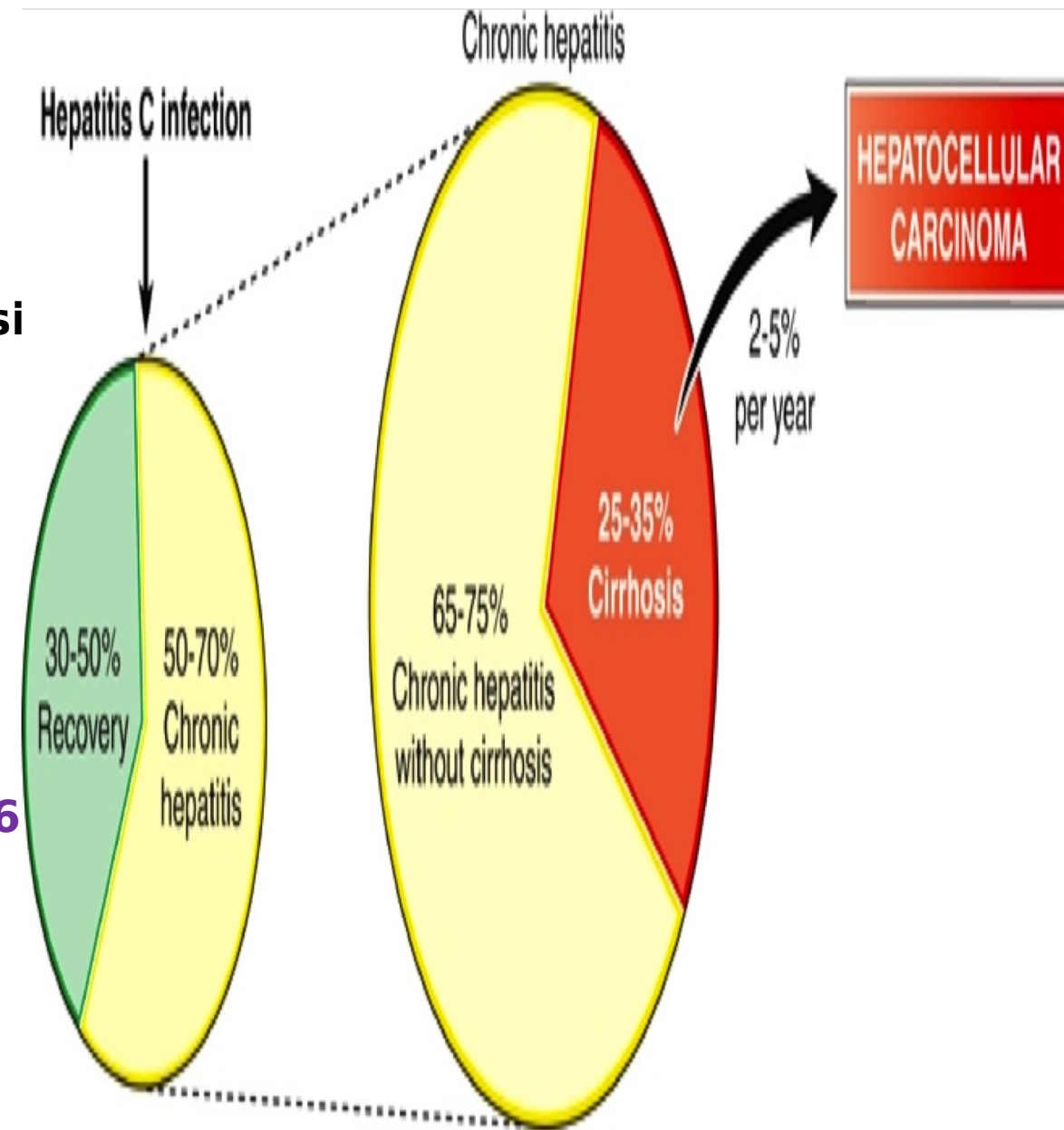
2-Chronic hepatitis (50-75 % in adults)

a.Definition : Persistence of viral genome in blood ≥ 6

b.Determinant : adequacy of **CTLs**.

4-Liver cirrhosis

5-Hepatocellular carcinoma



Clinical features of HBV & HCV

	HBV	HCV
A-Incubation period	<u>1.5 months</u>	<u>2 weeks</u>
B-Symptoms & Signs	Symptoms are <u>more severe</u> 1-Fever, anorexia & vomiting 2-Jaundice, dark urine & pale stools 3-Enlarged & tender liver	80% are <u>asymptomatic</u>

SIGNS AND SYMPTOMS OF HEPATITIS-B

- Jaundice
- Fever
- Fatigue in a short period
- Abdominal Pain
- Gastrointestinal problems
- Loss of appetite



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Review of Medical Microbiology and Immunology.

Warren Levinson , Thirteenth Edition.

Chapter 41 (P 331-341).

